PATENT

Attorney Docket No.: 017473-001110US

EXPEDITED EXAMINING PROCEDURE
ART UNIT 1655

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Glenna C. Burmer, *et al.*

Application No.: 09/292,758

Filed: April 14, 1999

For: NUCLEIC ACID SEQUENCES AND PROTEINS ASSOCIATED WITH AGING

Examiner: B. Sisson

Art Unit: 1655

AMENDMENT AFTER FINAL

Box AF
Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the Office Action mailed July 31, 2001, Applicants respectfully request reconsideration in view of the following remarks and amendments. A petition to extend the time for response for three months, from October 31, 2001 to January 31, 2002, is submitted herewith. Also submitted herewith is Notice of Appeal. Please amend the above-identified application as follows:

IN THE SPECIFICATION

Please amend the specification on page 31, lines 22-38 as follows:

The cell suspension is generally centrifuged and the pellet containing the inclusion bodies resuspended in buffer which does not dissolve but washes the inclusion bodies, *e.g.*,, 20 mM Tris-HCl (pH 7.2), 1 mM EDTA, 150 mM NaCl and 2% TRITON-X-100™, a non-ionic detergent. It may be necessary to repeat the wash step to remove as much cellular debris as possible. The remaining pellet of inclusion bodies may be resuspended in an appropriate buffer (*e.g.*,, 20 mM sodium phosphate, pH 6.8, 150 mM NaCl). Other appropriate buffers will be apparent to those of skill in the art.

IN THE CLAIMS:

Please amend claims 11 and 38 as follows.

11. (once amended) The isolated protein of claim 8 which is encoded by SEQ ID NO:2.

38. (once amended) A kit for detecting whether a cell is G0-arrested, said kit comprising:

a probe which comprises a polynucleotide sequence selected from the group consisting of SEQ ID NO:1, 2, 38, 55, 61, 67, 69, 70, and 73; and

a label for detecting the presence of said probe.

REMARKS

With this amendment, claims 1-3, 6-11, 29, 31-33, 38, 39, 55, and 62 are pending in the present application and under examination. Claims 11 and 38 is amended. Appendix A provides the version with markings to show change. Appendix B shows all pending claims currently under examination.

Status of the specification

The specification has been amended to capitalize the trademark TRITON-X-100™ wherever it appears and to recite generic terminology. Applicants therefore respectfully request that the objection be withdrawn.

Status of the claims

Claim 11 was amended to recite "SEQ ID NO:2. This amendment adds no new matter.

Claim 38 was amended to recite a polynucleotide sequence "selected from the group consisting of SEQ ID NO:1, 2, 38, 55, 61, 67, 69, 70, and 73." This amendment adds no new matter. Support for this amendment can be found, e.g., in the specification on pages 61-65.

Rejection under 35 U.S.C. § 112, first paragraph: written description

"Positive recitation of specific sequences"

Claims 1-3, 6-11, 13, 14, 29-31, 38, 39, 55, 56, 62, and 63 were rejected as allegedly containing subject matter that was not described in the specification as originally filed. In the Office Action, the Examiner observed that the purpose of the written description requirement is to convey to one of skill in the art that the inventor was in possession of the invention as of the filing date. The rejection then stated that "[w]hile some of the claims place limits on the percent variability of the various nucleic acid sequences, the specification has not been found to provide an adequate written description of same to the extent that it reasonable conveys that applicants was in possession of such innumerable variants." December 6, 2000 Office Action, page 3. However, Applicants respectfully point out that the claims comply with the written description requirement, as described below, because each claim "includes the positive recitation of specific nucleic acid sequences." July 31, 2002 Office Action, page 3.

Applicants first note that claims 1, 2, and 3 recite an isolated nucleic acid that encodes a protein that "specifically binds to antibodies raised against a protein encoded by SEQ ID NO:1." Applicants further note that claim 6 recites an isolated nucleic acid that is "at

least about 80% identical to a nucleic acid sequence as set forth in SEQ ID NO:1." Applicants further note that claim 7 recites an isolated nucleic acid that "hybridizes to a nucleic acid having a sequence as set forth in SEQ ID NO:1 under stringent conditions." Applicants also note that claim 8, 9, and 10 recite an isolated nucleic acid that encodes a protein that "specifically binds to antibodies raised against a protein encoded by SEQ ID NO:2."

Applicants note that claim 11 now recites a nucleic acid which is "encoded by SEQ ID NO:2." Applicants also note that claim 38 now recites a sequence selected from the group consisting of "SEQ ID NO:1, 2, 38, 55, 61, 67, 69, 70, and 73." This claim therefore now recites the sequences that the Examiner indicated met the written description requirement. To the extent that the rejection applies to the claims as amended, Applicants respectfully traverse.

The claims fully comply with the requirements for written description as set forth in *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997). As described by the Federal Circuit in *Lilly*, "[a] description of a genus of cDNAs may be achieved by means of . . . a recitation of structural features common to the members of the genus . . . ." *Lilly*, 43 USPQ2d at 1406. Furthermore, the court in *Fiers v. Revel* stated that an adequate written description "requires a precise definition, such as by structure, formula, chemical name, or physical properties." *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). The claims set forth structural elements based on reference nucleic acid or amino acid sequences, e.g., either (1) reference amino acid sequences against which antibodies are raised, which specifically bind to the claimed sequences; (2) reference nucleic acid sequences to which the claimed sequences have a specified percent identity; and (3) reference nucleic acid sequences to which the claimed nucleic acids hybridize under specified hybridization conditions. Therefore, the claimed sequences are thereby defined via shared physical and structural properties.

As described above, the present invention relates to the discovery of nucleic acids and proteins associated with the aging process. The senescence-associated nucleic acids and the proteins that they encode are claimed by reference to shared structural features, i.e., nucleic acid and amino acid sequences. As described above, the claims provide sequences that

bind to antibodies raised against the reference sequences, hybridize to the reference sequences, or have a specified identity to the reference sequences.

The ability of a particular nucleic acid to hybridize under *given conditions* to a reference nucleic acid is a physical/structural property of the nucleic acid, because it relies upon the nucleotide sequence of the molecule (*see, e.g.*, Sambrook, *Molecular Cloning: A Laboratory Manual*, pp. 9.47-9.51 (2nd ed. 1989); *see also* Stryer, *Biochemistry*, pp. 573 (2nd ed. 1975)). As described in Stryer, the transition between hybridization and melting of complementary nucleic acid strands is abrupt and largely sequence dependent. When the temperature of hybridization is provided, one of skill in the art would be able to predict whether or not a given sequence would hybridize to a reference sequence (*see, e.g.*, equations provided in Sambrook, *supra*). Moreover, in the same light, the percent identity of a nucleic acid to a reference sequence is a structural feature, as it relies entirely on the sequence of the molecule. Furthermore, the ability of a antibody to specifically bind to an amino acid sequence is a structural feature, as it relies entirely on the sequence of the molecule.

In the present application, Applicants have provided both reference nucleotide and amino acid sequences, as well as specified hybridization conditions and sequence analysis algorithms. Furthermore, the trait of "specific binding" by an antibody is defined in the specification and would be clearly understood by one of skill in the art (see, e.g., specification, page 19, lines 4-22). As required by the standard set forth in *University of California v. Eli Lilly*, these structural features are common to all of the members of the claimed nucleic acids and the proteins they encode. The conserved sequences encoding these structural features, and the given conditions under which the claimed sequences would hybridize to such reference sequences or have a specified identity to such sequences or bind to antibodies raised against such sequences "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (*see*, Office Action, page 4, *quoting Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 111, 1116 (Fed. Cir. 1991)). The specification thus appropriately describes the claimed senescence associated nucleic acid and protein genus using structural/physical features, as required by the court in *University of California v. Eli Lilly*. As such, Applicants respectfully request that the Examiner withdraw the rejection.

"Chip"

Claims 31 and 32 were rejected as allegedly containing subject matter that was not described in the specification as originally filed. In the Office Action, the Examiner observed that the purpose of the written description requirement is to convey to one of skill in the art that the inventor was in possession of the invention as of the filing date. July 31, 2001 Office Action, page 2. However, the Examiner goes on to state that "[s]upport for solid supports, in a general fashion, is found at page 38, line 24, bridging to page 39, line 20. A review of this passage is found to contain numerous suggestions as to how one may proceed in developing such a device . . . ." July 31, 2001 Office Action, page 3. Applicants respectfully traverse the rejection.

The standard for meeting the written description requirement is not whether the Applicants are "in possession of such a device." The standard is whether Applicants are in possession of the invention: "to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention." MPEP § 2163.02. According to the MPEP, Applicant can show possession of the invention in a number of ways, including "by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams and formulas . . . ." *Id.* As stated by the Examiner, the present specification on page 38 to page 39 clearly provides support for solid supports, and describes how to develop a device such as a chip comprising an array of sequences. As chips and other devices comprising probes are well known to those of skill in the art, the description of the invention in the application as filed is sufficient to meet the written description requirement.

Applicants further note that the MPEP states that "there is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed. Consequently, rejection of an original claim for lack of written description should be rare." MPEP § 2163.0. Claims 31 and 32 are original claims, and should be accorded a strong presumption of adequate written description. Applicants therefore respectfully request that the rejection be withdrawn.

Rejection under 35 U.S.C. § 103

Claims 29-33, 38, 39, 55, and 62 were rejected as allegedly obvious over Thompson in view of Hillier *et al.* (Accession No. N53466), and further in view of Sosnowski *et al.* Hillier discloses an EST sequence that correspond to SEQ ID NO:55 but provides no function for that sequence, and specifically fails to teach or suggest that the EST plays a role in cellular senescence. Thompson discloses generic kits comprising probes. Sosnowski *et al.* discloses a generic method and electronic device for transport and hybridization of DNA. Applicants respectfully traverse the rejection.

In order to establish a prima facie case of obviousness, three basic criteria must be meet: (1) there must be a suggestion or motivation, either in the references themselves, or in the knowledge generally known to one of skill in the art, to modify or combine the references; (2) there must be a reasonable expectation of success; and (3) the prior art references must teach or suggest all the elements of the claims. MPEP §2142.

Hillier *et al.* discloses an EST of unknown function, and the remaining references disclose generic kit and hybridization methods. The present application for the first time disclosed that SEQ ID NO:5 was involved in cellular senescence. As none of the cited references teach or suggest that SEQ ID NO:55 is involved in cellular senescence, the references either alone or in combination fail to make obvious the claimed invention. Applicants therefore respectfully request that the rejection be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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